South African Medical Journal
Suid-Afrikaanse Tydskrif vir Geneeskunde

Vol. 24, No. 46 Cape Town, 18 November 1950 Weekly 2s

CYANOSIS DUE TO COLD AGGLUTININS

A. T. Neser, B.Sc., M.B., Ch.B.
South African Institute for Medical Research, Bloemfontein
and
I. Sacks, M.B., Ch.B., M.D.
Bloemfontein

Cold agglutinins appear regularly in certain diseases and sporadically in others. Usually no signs or symptoms are caused by the presence of these agglutinins. Occasionally intravascular haemolysis occurs and causes haemolytic anaemia. Cyanosis due to capillary obstruction by the agglutinated cells is not a frequent phenomenon.

A middle-aged male, a miller by occupation, was referred by Drs. van Schalkwyk and Dippenaar of Bethlehem with the following history: During the past week he had several attacks of cyanosis affecting the skin over the whole of his body. Taking a warm bath or getting into a warm bed caused complete disappearance of the cyanosis. Physical examination failed to reveal any abnormality in the thoracic and abdominal cavities. He denied the use of narcotics or any other drugs. Treatment with Aminophyllin, Papaverine and Benadryl did not ameliorate the condition. Venous blood was collected but 'clotted' at once and smears could not be made.

Dr. Sacks examined the patient on 25 August 1949 and confirmed the presence of cyanosis and the absence of other clinical signs. The patient had no physical discomfort. He went to see a doctor only because he found the dark blue colour of his face embarrassing.

The patient attended at the Institute the same day. The first attempt to make smears was not successful as the red cells formed clumps up to 1 mm. in diameter on coming into contact with the cold glass slide. By working very rapidly the first half of the smear could be made, but agglutination occurred before the smear could be completed. The syringe and slides were then heated in the 37° C incubator and perfectly satisfactory smears could be made. The results of the laboratory investigations are summarized.

Cold Agglutinins. Cold hetero- and auto-agglutinins were present to a titre of 1 : 1,024. At 37° C agglutinins were present to a titre of 1 : 8.

Malta Fever. Serial dilutions of 1 : 25 to 1 : 3,200 gave negative results with *Br. melitensis* and *Br. abortus* suspensions. A guinea-pig was inoculated with 5 c.c. blood. No rise in the Brucella titre occurred within six weeks.

Typhoid and Typhus. The Widal and Weil-Felix reactions were negative.

Syphilis. The Ide and Eagle serologic tests were negative. The Donath-Landsteiner test was negative.

Blood. Haemoglobin, 18 gm. %. Erythrocytes 6,130,000 per c.mm. Leucocytes 12,200 per c.mm. Polymorphs 74%. Mononuclears 5%. Lymphocytes 20%. Eosinophils 1%. The platelets were not diminished. Bleeding time, 45 seconds. Coagulation time, 4½ minutes. No sulph-or methaemoglobin was present. Icteric index, 5.

Urine. An occasional leucocyte was present in the centrifugalized deposit. There was no urobilinogen and spectroscopic examination for haemoglobin derivatives was negative.

Some of the serum separated at 37° C was forwarded to the Human Serum and Rickettsial Laboratory and Dr. Zoutendyk reported as follows:

Group O, Rh-positive C+ D+. The direct and indirect Coomb's tests were negative. This serum contains very weak irregular agglutinins active at 37° C and hetero-cold agglutinins to a titre of 1 : 2,000 as tested against random Group O, Rh-positive and negative cells. It gave negative complement fixation tests for louse, murine and tick typhus, for Q fever and for relapsing fever.

The patient was admitted to hospital and the previous clinical findings were confirmed. Warmly covered up in bed his skin was a uniform pink colour. On immersion of a limb in cold water it became cyanosed. This cyanosis disappeared when the limb was placed in warm water. On sitting up in his pyjamas only, his

whole body becomes covered with cyanotic areas three to four inches in diameter. The cyanosis is so intense that it resembles patches of ecchymosis. X-ray examination of his chest revealed no abnormality. He was treated with Benadryl and Aureomycin with no improvement of the condition and was discharged from hospital after ten days.

On 20 October 1949 the serologic investigations were repeated. With the exception of the Widal, the results were identical with those previously reported. The Widal was strongly positive but enquiry elicited that he had been injected with T.A.B. vaccine some weeks before.

The patient was next seen 8 February 1950. Clinically his condition was the same but in addition he complained of tenderness over his liver area. The results of the laboratory tests performed on this occasion are summarized:

Agglutinins. Cold auto- and hetero-agglutinins are present up to a titre of 1 : 1,024. No auto- or hetero-agglutinins could be demonstrated at 37° C.

Erythrocyte Agglutinability. The red cells were not agglutinated when tested with eight random sera.

Syphilis. The Ide, Eagle and Kline cardiolipin tests were negative.

Blood. Haemoglobin, 20.7 gm. %. Erythrocytes, 6,170,000 per c.mm. Leucocytes 13,100 per c.mm. Polymorphs 74%. Monocytes 1%. Lymphocytes 25%.

Liver Tests.

Thymol flocculation +++.	Globulin 3.9 gm. %.
Cephalin cholesterol flocculation ++++.	Alkaline phosphatase 8.9 units.
Prothrombin index 100%.	Acid phosphatase 1.2 units.
Total protein 7.5 gm. %.	Icteric index 5.
Albumin 3.6 gm. %.	Urine urobilinogen, Absent..

Urine. The centrifugalized deposit showed calcium oxalate and uric acid crystals with an occasional leucocyte.

During May and again during June we were informed by Drs. Dippenaar and van Schalkwyk that the patient no longer had any pain or tenderness over his liver, that the cyanosis was unchanged and that he had no other complaints.

DISCUSSION

Patients with such high cold agglutinin titres fall into one of three groups:

A. Severe anaemia.
B. Haemolytic anaemia or transfusion reactions.
C. Acute or chronic infective conditions.

As there is no anaemia, only the infective conditions have to be considered. Cold agglutinins are commonly present in pulmonary tuberculosis and virus pneumonia. It may occur in brucellosis (personal communication from Dr. Zoutendyk). Engleson and Grubb [1] report a case where cold agglutinins as well as abnormal agglutinability of the red cells occurred in association with a pyogenic infection.

This patient had a slight leucocytosis but there was no other evidence of an infection. The absence of a raised temperature, the negative roentgenological findings and the general feeling of well being did not point to the presence of an infection. The positive flocculation tests for liver disease are related to an increase in gamma globulin which is increased in any antibody response whatever and do not necessarily point to liver disease.

We are therefore unable to state what caused the production of these cold agglutinins which have now been present in his serum for nearly 10 months.

SUMMARY

A case is reported where cold agglutinins caused reversible intravascular agglutination with resultant cyanosis. There was no evidesce of intravascular haemolysis and the cause of the condition could not be determined.

REFERENCE

1. Engleson, G. and Grubb, R. (1949): Amer. J. Clin. Path., **19**, 782.

TRACHOMA

AUREOMYCIN (OILY SUSPENSION) IN ITS OUT-PATIENT TREATMENT

A PRELIMINARY REPORT

R. A. TROPE, M.B., B.CH. (RAND), D.O.M.S., R.C.P. & S.*
Krugersdorp

Because trachoma is exceedingly common in South Africa, a report by Duke-Elder, Ainslie and Boase (1950) of encouraging results in eight cases of trachoma treated by aureomycin borate solution is of great importance.

Previously Moutinho Grilo and Moura (1949), in Portugal, using drops and an ointment continuously at 2-hourly intervals day and night for two to six days, successfully treated 15 cases of trachoma and Braley and Saunders (1948-49) successfully treated one case of trachoma stage III with drops of aureomycin borate.

Following these reports it was decided to use aureomycin drops in the treatment of trachoma in this Hospital. The borated salt of aureomycin, prepared according to the method of Braley and Saunders and also an ophthalmic solution prepared by the manufacturers were used.

Results were unfortunately very disappointing and I seriously considered giving up this method of treatment and only using it as an adjunct to previously established

* Ophthalmic Registrar, Krugersdorp Hospital.

methods. Following further investigation of the cases treated, however, it was noticed that:—

(*a*) In almost all these cases the patients had been treated as weekly out-patients;

(*b*) The ophthalmic solution of aureomycin has an antibiotic activity varying from 12 to 48 hours. These two factors suggested further trial of a solution which would retain its potency longer, as Native patients resist hospitalization, find difficulty in attending a daily Out-Patient Clinic owing to economic factors and often live long distances from Hospitals.

After various trials a suspension of aureomycin hydrochloride in castor oil was used in the following form:—

Aureomycin hydrochloride 50 mg.
Ol. Ricini 10 c.c.
Shake before use.
Sig. To be instilled into the eyes every hour.

This suspension was not more irritating than the borated aqueous solution.

Eight cases of typical trachoma varying from stages I to IV were treated with extremely gratifying results. In seven cases the patients were treated as out-patients reporting once a week only.

Although this number is small, in view of the importance of this problem and the marked difference in results when using the oily suspension for out-patients, I feel it is worth reporting them.

Although only undoubted cases of trachoma are described, this vehicle has also proved useful in several doubtful cases as well as in non-trachomatous conditions, notably herpes simplex, where the organism was penicillin-resistant. It has also proved an extremely simple and cheap method of dispensing aureomycin for ophthalmic use.

A most important aspect of this treatment is that it allows domiciliary treatment. As the suspension retains its antibiotic activity, a two-weeks' supply can be dispensed (at a cost of 1s. to 2s. to the authorities) and if deemed advisable almost any amount can be prepared in the full confidence that the preparation will retain its potency unimpaired.

With the aqueous solution, on the other hand, even if we assume that a daily supply can be dispensed inexpensively and without wastage (at present an impractical procedure) this will still necessitate either hospitalization of all patients or their daily attendance at a clinic—procedures which are obviously unsound economically and practically both for the taxpayer and the patient. Especially is this so in the patients who suffer from this blinding disease, those patients in the rural areas whom it is planned to reach by mobile units and where daily observation is an impossibility.

CASE REPORTS

Case 1. This patient, a European female aged 21, mongoloid, was suffering from trachoma stage III. There was no pannus but signs of previous vascularization were present. Her eyes were painful, there was a mucopurulent discharge and photophobia. After using 10 c.c. there was a marked improvement in her condition and following a further 10 c.c. of the drops her tarsi were smooth and the condition clear. The signs of previous scarring were naturelly still present.

Case 2. A Coloured male aged 20 presented typical stage I signs and symptoms. He was treated for three weeks with Sulphacetamide 30% Gutt. penicillin G 10,000 units per c.c. and Sulphadiazine by mouth. During treatment he progressed to stage II, presenting both follicles and papillary enlargement of the tarsal conjunctivae. He was then put on to aureomycin in oily suspension with dramatic results. Within a week his condition was almost normal and a week later the conjunctivae were smooth and shiny and the early corneal vascularization had totally disappeared. This was the only case presenting trachoma in such an early stage.

Case 3. A non-European female aged 14 years first presented with trachoma stage IV and early entropion and trichiasis of the right eye. She was treated with Sulphacetamide and Sulphadiazine with no effect for three weeks. She was then admitted for operation and treated with oily aureomycin suspension for 14 days pre-operatively and then discharged as clinically cured. Amazingly enough the entropion had disappeared. I feel that in this case, in spite of the obvious scarring, the entropion was spastic in origin, following on the blepharospasm.

Case 4. A non-European female aged 23 presented as trachoma stage III with marked pannus reaching to the pupillary aperture in the right eye. She complained of photophobia and pain. A purulent discharge was present; also old scars of the tarsal conjunctivae with papillary enlargement and typical pannus which was exceptionally well marked. After seven days of treatment the conjunctival condition was normal and the pannus had practically cleared. This regressed in the same way as pannus usually does but only much more rapidly and unexpectedly as the pannus was advancing when treatment with oily auremycin commenced.

Cases 5-8. These were all straight-forward cases of trachoma stage III which cleared up within 7-10 days of treatment.

SUMMARY

Eight cases of trachoma were treated with an oily suspension of aureomycin hydrochloride with extremely encouraging results.

A simple method of preparing aureomycin for ophthalmic use, where the antibiotic activity of the drug remains unimpaired, is described.

In addition, a simple means of reaching and treating cases of trachoma in rural areas at great distances from hospitals and where daily observation cannot be maintained, is now available.

I wish to acknowledge with thanks the help and encouragement I received in this investigation from Dr. I. Frack, Superintendent of this Hospital, Dr. J. Taussig, Head of the Department of Ophthalmology, Dr. O. Cronje, House Surgeon in this Department and Mr. O. L. Raff, Dispenser.

REFERENCES

1. Duke-Elder, Sir Stewart, Ainslie, D. and Boase, A. J. (1950): Brit. J. Ophthal., **34**, 30.
2. Braley, A. E. and Saunders, M. (1948): J. Amer. Med. Assoc., **138**, 426.
Braley, A. E. and Saunders, M. (1949): Amer. J. Ophthal., **32**, 119.

South African Medical Journal
Suid-Afrikaanse Tydskrif vir Geneeskunde

VAN DIE REDAKSIE

VERSLAAFDHEID AAN BARBITURAATVERDOWINGSMIDDELS

'n Onlangse verslag vestig die aandag op die verskynsel van verslaafdheid by sommige persone wat gereeld 'n barbituraat-verdowingsmiddel gebruik.[1] Dit is 'n ware verslaafdheid wat by vatbare persone voorkom en is nie bloot 'n groter afhanklikheid van die verdowingsmiddel nie. Die barbituraat-verdowingsmiddels is dus gewoontevormend in die ernstigste sin en hulle moet moeiliker bekombaar gemaak word vir dié mense wat misbruik van hulle kan maak. Die leke-publiek het reeds al die gevaar ontdek van abnormaal groot dosisse te neem. Barbituraat-verdowingsmiddels word met sorgbarende veelvuldigheid in gevalle van pogings tot selfmoord gebruik.

Die kroniese gebruiker van 'n barbituraat-verdowingsmiddel openbaar dieselfde eienskappe wat by 'n verslaafde aan narkotiese verdowingsmiddels teengekom word. Hy kan groot hoeveelhede van die verdowingsmiddel verduur waarvan hy emosioneel en fisies afhanklik is. Dit is so moeilik om verslaafdes aan barbiturate van gebruik van die verdowingsmiddel te weerhou as wat dit is om iemand wat aan alkohol of morfien verslaaf is te genees. Skielike onthouding van die barbituraat lei tot strawwe geestesnood en fisiese simptome.

'n Pasiënt wat vir 'n lang ruk van die verdowingsmiddel gebruik maak, word verward en sy verstandelike vermoë word aangetas. Hy kan oogtrilling, belemmerde spraak, bewing, disdiadokokinesis, hipotonia en 'n slingergang ontwikkel.

Wanneer die verdowingsmiddel van so 'n kronies bedwelmde persoon ontneem word, volg 'n kenmerkende reeks simptome. Die tekens van bedwelming neem af maar die pasiënt word swak, hy kan nie slaap nie, toon tekens van groot angs, verloor aptyt, word mislik en vomeer. Daar is vinnige gewigsverlies, 'n styging in die pols- en asemhalingsnelheid, verhoging van die bloeddruk, trekkings en delirium wat soos alkoholiese *delirium tremens* gekenmerk word deur rusteloosheid, angs, koors, slaaploosheid, verwarring, waanbeelde en gehoors- en gesigshallusinasies. Die verdowingsmiddel moet dus by die behandeling van kroniese barbituraatbedwelming geleidelik weggeneem word indien die verskyning van ontnemingsimptome vermy moet word.

Kroniese barbituraat-bedwelming is in geneeskundige literatuur verwaarloos. Daar is nie vermoed dat die skielike wegneem van barbituraat-verdowingsmiddels van 'n verslaafde strawwe ontnemingsimptome veroor-

1. Isbell, H. (1950): Ann. Int. Med., **33**, 108.

EDITORIAL

ADDICTION TO BARBITURATE DRUGS

A recent report draws attention to the occurrence of addiction in some persons who regularly use a barbiturate drug.[1] It is a true addiction which occurs in the susceptible person, and not merely a greater dependence on the drug. The barbiturate drugs, therefore, are habit-forming in the gravest sense and require to be made less easily available to such people as may misuse them. The lay public has already discovered the dangers of acute overdosage. Barbiturate drugs are employed with distressing frequency in cases of attempted suicide.

The chronic user of a barbiturate drug presents those features encountered in any narcotic addiction. He can tolerate large quantities of the drug, upon which he is emotionally and physically dependent. It is as difficult to restrain barbiturate addicts from using the drug as it is to cure an alcoholic or a morphine addict. Abrupt withdrawal of the barbiturate drug results in severe mental distress and physical symptoms.

A patient who uses the drug for a long time becomes confused and his mental ability is impaired. He may develop nystagmus, dysarthria, tremor, dysdiadokokinesis, hypotonia and an ataxic gait.

When such a chronically intoxicated person is deprived of the drug, a characteristic train of symptoms follows. The signs of intoxication diminish, but the patient becomes weak, he cannot sleep, shows great anxiety, loses his appetite, becomes nauseous and vomits. There is rapid weight loss, elevation of pulse and respiratory rates, increase in blood pressure, convulsions and development of a delirium which, like alcoholic delirium tremens, is characterized by agitation, anxiety, fever, insomnia, confusion, delusions and auditory and visual hallucinations. The drug must, therefore, be withdrawn gradually in treating chronic barbiturate intoxication, if the occurrence of deprivation symptoms is to be avoided.

Chronic barbiturate intoxication has been neglected in the medical literature. It was not suspected that the abrupt withdrawal of barbiturate drugs from an addicted person caused gross abstinence symptoms, until the

1. Isbell, H. (1950): Ann. Int. Med., **33**, 108.

saak nie totdat dit in 1947 aangemeld is dat aanvalle soos dié van vallende siekte dikwels na so 'n ontneming voorkom.[2]

Soos in die geval van verslaafdheid aan alkohol en narkotiese verdowingsmiddels is die vernaamste voorbestemmingsfaktor van verslaafdheid aan barbiturate die aanwesigheid van 'n persoonlikheidsgebrek. Iemand wat òf psigo-neuroties òf 'n gestelpsigopaat is, sal waarskynlik daaraan verslaaf raak indien hy op 'n geskikte tyd daarmee bekend gemaak word. Baie gevalle van kroniese verslaafdheid aan barbiturate is die gevolg van die toediening van die verdowingsmiddel deur geneeshere wat nie daarvan bewus is dat verslaafdheid voorkom nie. Die verdowingsmiddel kon vir slaaploosheid voorgeskryf gewees het; later word dit nie as 'n slaapmiddel gebruik nie maar om bedwelming te weeg te bring. Verslaafdes aan alkohol kan die middel gebruik met die uitdruklike doel om bedwelming te weeg te bring eerder as om senuweeagtigheid of slaaploosheid te verlig. Baie psigopate gebruik barbiturate om die uitwerking van alkohol te versterk.

Weens hulle skadelikheid moet die verkoop van barbituraat-verdowingsmiddels strenger deur die wet beperk word. Indien die geneesheer daarbenewens bewus is dat verslaafdheid voorkom, kan hy in baie gevalle die geestelike verwarring en ekonomiese onvermoë waaraan 'n verslaafde aan verdowingsmiddels ly, verhoed deur versigtig te wees by die voorskryf van barbituraat-verdowingsmiddels vir vatbare persone.

2. Osgood, C. W. (1947): J. Amer. Med. Assoc., **133**, 104.

frequent occurrence of epileptiform seizures following such withdrawal was reported in 1947.[2]

As in the case with alcohol and narcotic drug addiction, the most important predisposing factor to barbiturate addiction is the presence of a personality defect. A subject who is either psychoneurotic or a constitutional psychopath is likely to become addicted if introduced to the drug at an appropriate time. Many cases of chronic barbiturate addiction result from administration of the drug by physicians who are unaware that an addiction occurs. The drug may have been prescribed for insomnia; later it becomes used not as a means of inducing sleep but as a means of producing intoxication. Alcoholics may use the drug with the direct aim of causing intoxication rather than to relieve nervousness or insomnia. Many psychopaths use barbiturate drugs to reinforce the effects of alcohol.

Because of their harmfulness, the sale of barbiturate drugs ought to be restricted more closely by law. Moreover, if the medical practitioner is aware that addiction occurs, he may, in many cases, by using care in prescribing barbiturate drugs to susceptible persons, prevent the mental disorganization and economic incapacity which a drug addict suffers.

2. Osgood, C. W. (1947): J. Amer. Med. Assoc., **133**, 104.

MEDICO-LEGAL SECTION

ACTS PERTAINING TO THE CALLING OF A MEDICAL PRACTITIONER

IN THE SUPREME COURT OF SOUTH AFRICA

(TRANSVAAL PROVINCIAL DIVISION)

5 June 1950.

H. SCHAEFER AND F. LEWIG v. REX

Millin, J.: The appellants in this case are two women, each of whom holds the degree of Doctor of Medicine of a German University, but neither of them is entitled to be or is registered as a medical practitioner under the law of the Union. They were charged with contravening section 34 (*a*) and (*b*) of Act 13 of 1928 as amended. The first count relates to section 34 (*a*) and it sets out that during the period between 13 April 1949 and 30 June 1949, at a stated address, the appellants, not being registered as medical practitioners did wrongfully and unlawfully, for gain, practise as medical practitioners or perform acts specially pertaining to the calling of medical practitioners. That is the first count. The second count alleges when read with the particulars supplied, that they contravened section 34 (*b*) of the same statute because they used a name, title, description or symbol indicating or calculated to lead persons to infer that they are registered as medical practitioners under the Act. That is the second count. The evidence relating to that is far simpler than that relating to the first count and I shall deal with it first. I have said that the two appellants do hold the degrees of Doctor of Medicine. If they had merely described themselves as 'doctor so and so' then on the authorities that mere fact would not have brought them within the mischief of this sub-section; for instance, if they had cards on which they described themselves as Dr. Schaefer or Dr. Lewig. But the evidence is that they had a plate outside the premises where they carried on their occupation, 71 Park Court, Twist Street, Johannesburg, on which the following legend appeared:

Continental Institute for Skin Treatment,
Dr. H. Schaefer.
Dr. F. Lewig.

It seems to me clear that the collocation of the title 'Doctor with an institute for skin treatment is cer-

tainly calculated to lead those who read this legend to infer that they have to do with duly registered medical practitioners.

Mr. *Coleman* has suggested that the word 'Institute' might dispel the belief that these are medical practitioners, but I think on the contrary the word 'Institute' is just the kind of thing to lead to such a belief. One knows or reads of Institutes for the study and treatment of various diseases all over the world and that is why I think that the collocation of the title 'Doctor' with the description of a business as an institute for skin treatment is calculated to lead to the inference that one is dealing with duly registered medical practitioners. Therefore, as regards the second count, it is plain that the appeal must fail.

The first count is based on the evidence of a woman who took a child to the appellants for the treatment of a skin affection from which this child was manifestly suffering. What this woman said was not only admitted by the appellants in their evidence but expanded. Mr. *Coleman* has fairly said that they gave their evidence with a great deal of candour. The first appellant in her evidence-in-chief after dealing with the inscription outside the premises said this: 'Whenever people come I usually tell them that I am not a registered S.A. medical practitioner'. I ought to mention that attention was drawn to that in connection with the second count, but the point was not pressed that you can escape conviction for using symbols of this kind merely because when your customers are inside your premises you explain that you are not really a registered medical practitioner. Then the witness goes on: 'We never do any examinations and never charge for examinations. We treat people who come to us. From experience we can see what it is all about, looking at skin. Apart from a visual examination we do nothing to the skin in order to make up our minds. If any other diagnosis were necessary we send them to medical practitioners. We give no prescription or injection. Treatment consists of painting, massaging. We don't apply compresses. In some cases our treatment is similar to "Beauty" treatment.' Then in cross-examination she says this: 'When Mrs. Reynard's (that is the complainant) daughter came to us first I asked where the infection was as I knew she was suffering from eczema and looked at the affected parts and painted them. Painting is a form of treatment for eczema. There are very many types of eczema. Each has its own characteristic and appearance. Each type requires a different treatment. As a doctor you require experience to say which type it is. That is to certain extent. There are different schools of thought about eczema. Some medical men who think that certain skin troubles are caused by infection and are contagious and others put the skin trouble under heading of eczema which is not contagious. You must have some knowledge and experience before you can say which kind of eczema you are looking at. We treat not only eczema but other skin troubles as well. When we have decided on the type of eczema or skin trouble then we decide on the treatment. The supply of ointments and powder belongs to the treatment. I followed this procedure in regard to this little girl. Painting is first treatment for every kind of eczema.' Then the second appellant, without going into details, identified herself in every way with what the first appellant had said. Mr. *Coleman* in his very interesting and attractive argument has conceded that all this that I have read might well be the procedure of any orthodox medical practitioner. But he says, the first thing that the Crown has to prove is that the acts which are complained of are acts which specially pertain to the calling of a medical practitioner and he has shown us that in the case of *Rex* v. *Smith* (1917, T.P.D. 206) at page 208 it was said by the then Judge President that where a person is charged with acting as a physician, as the law specifically says, performing such acts as specially belong to the calling of a medical practitioner it is clear that the onus is on the Crown to prove that only medical practitioners, and nobody else, perform such acts. For if not, they cannot specially belong to the calling of a medical practitioner. Then the learned Judge President went on to refer to the leading case of *Rex* v. *Greene* (1905, T.S.C. 595) where it was laid down that the functions of a medical practitioner consist in diagnosing the malady, advising the patient, and prescribing for the complaint. 'Prescribing' includes also treatment as pointed out in Smith's case by Mr. Justice Bristowe. He said he preferred the word 'treating' instead of the word 'prescribing', and then prescribing would be part of the treatment. What Mr. *Coleman* has argued is that, while there might be some cases where one could see without any doubt and without any evidence that what has been done is something which specially pertains to the calling of a medical practitioner, that is not true to all cases. He says there are cases in which the Court takes judicial notice of the fact that here is something specially pertaining to the calling of a medical practitioner, but the Court cannot take judicial notice of something which is not within the experience of ordinary people as specially pertaining to the calling of a medical practitioner. To my mind the most important part of this statement concerning what are acts specially pertaining to the calling of a medical practitioner, namely that they consist of diagnosis, diagnosing the malady, advising the patient and treating him, is the matter of diagnosis. Diagnosis means applying scientific knowledge to the ascertainment of what the disease is from which the patient is suffering. That is the fundamental thing that a medical practitioner does and when he has ascertained that to his satisfaction, he is in a position to give the necessary advice and to apply the necessary treatment. Mr. *Coleman's* argument is that we are dealing with a condition called eczema which we know is a skin disease, but he says it is not so far a matter of common knowledge that the Court ought to take judicial notice of the fact that it specially pertains to the calling of a medical practitioner to deal with this condition; to find out by examination that the trouble is in fact eczema and then to proceed further and to find out which one of the great variety of examples of eczema one has to deal with. Is that, he asks, a matter of which the Court can take judicial notice? Well, we know from the evidence that we are dealing with a disease and, I think it is a matter of common knowledge that it is a disease which is, although perhaps not fatal, perhaps not something that affects the general health, is an exceedingly troublesome matter which it

is very difficult to get rid of. I think most people have seen that. Now what did these people do? They were told that this child was suffering from eczema. They asked to see the affected part, they confirmed that the disease was indeed eczema, then they considered further what kind of eczema this was because they knew there were many varieties. To that they applied skill which there is no reason to doubt they in fact possessed. They say that knowledge and experience are both necessary in order to determine what kind of eczema you are looking at. Then they say that when they have decided on the type of eczema or skin trouble, they decide on the treatment. I myself feel no difficulty in coming to the conclusion that these are acts specially pertaining to the calling of a medical practitioner. They have nothing in common with the acts described in cases which have arisen for example where a man sells a pair of spectacles to a person who considers himself in need of spectacles; where a druggist is told by his customer that he has a troublesome cough and the druggist says 'Try this or that patent remedy' which he then sells him. Nor is the case at all like the case on which Mr. *Coleman* has placed some reliance, *Rex* v. *Williams* (1949 (4), S.A.L.R. 53). That was a case of a person who, for a small charge, administered an enema to a sick child. What had happened was that the accused came to the mother of this child, saw the child was sick and enquired whether an enema had been tried. On receiving the answer 'no' he offered to administer the enema and did so. The learned Judge who dealt with the case on review felt himself unable to say without evidence that the administration of an enema was something which purely belonged to the calling of a medical practitioner. That is a perfectly intelligible approach to the question, because as Mr. *Claasen* has said, the learned judge was dealing with an instrument or appliance which it is common to find in households, and there must be grave doubt whether it really needs a qualified medical practitioner to use such an instrument on the body of a sufferer. Apart from that I find nothing in the case of *Williams* to show that there was any attempt or pretence to diagnose. Then Mr. *Coleman* has invoked as an analogy the case of a hairdresser who recommends to his customer a hairwash or some ointment to apply to a scalp which he considers is too dry. He also referred to chiropodists and to people who call themselves beauty specialists and he asks: Can the Court take judicial notice of the fact that these people are doing things which may belong to the calling of a medical practitioner? The truth of the matter is that every case has got to be decided on its own facts. Analogies of this kind do not help unless you know exactly what the people concerned are doing. If a barber recommends a substance which will moisten the scalp, that is one thing. If he goes further and pretends to diagnose some skin disease which he is in a position to treat he may be contravening the law. Similarly a man may cut corns and make a charge: no one would say this was an act specially belonging to the calling of a medical practitioner, but if he goes further and performs something in the nature of a surgical operation he may well be contravening the law. Now in the present case the facts are all before us. We can see that the appellants have been diagnosing a disease. They ascertained by study and examination and by the application of their training and experience exactly what kind of disease it was and then determined the method of treatment and applying it. I cannot think that it requires any expert evidence to tell us that these who do this kind of thing are doing acts which specially pertain to the calling of a medical practitioner. I think on the first count too the appeal fails.

de Villiers, J.: I agree. I have nothing to add.

Millin, J.: The appeal is dismissed and the conviction and sentence are confirmed.

THERAPEUTICS BULLETIN

COMPILED BY
FLORENCE V. STEPHEN-LEWIS
Department of Pharmacology and Therapeutics, University of the Witwatersrand, Johannesburg

GASTRO-INTESTINAL SYSTEM

Recent advances in therapeutics of the gastro-intestinal tract are concerned with treatment of gastro-enteritis and of typhoid fever with antibiotics, and with the etiology and treatment of peptic ulceration.

USE OF ANTIBIOTICS IN ENTERITIS

Shigella Enteritis. A series of cases treated with Streptomycin, Aerosporin, Sulphadiazine, indicated that for relief of Symptoms, etc., the drugs were of equal value but the toxic effects of Aerosporin were sufficiently marked to preclude its use.

Chloramphenicol is effective *in vitro* against the Shigella group of organisms.

Typhoid Fever. Chloramphenicol (Chloromycetin) may be regarded as the drug of choice for this condition. Recent reports indicate that initial high dosage of 3.0 gm. orally, followed by 3.0 gm. daily results in a fall in temperature by lysis after 36 hours. This is accompanied by relief of Symptoms and the temperature is usually normal after 3 or 4 days. The dosage is reduced to 2.0 gm. daily for 6 to 10 days, a total 14-day treatment being the average required. If treatment is stopped earlier relapses may occur.

Complications of Chloromycetin Therapy. These include:

1. Excessive liberation of toxin due to rapid lysis of bacteria. This may be fatal.
2. Haemorrhage and perforation of the gut may occur in the early stage of treatment. Careful nursing and diet are therefore essential.
3. Vitamin deficiency may be produced rapidly following full doses of chloromycetin.
4. The recovery from the attack of fever may be uneventful but the patient may remain a carrier.

PARATYPHOID FEVER

Similar good results have been recorded in the treatment of paratyphoid fever: response to chloromycetin is rapid, but the faeces do not necessarily become free of bacteria.

Chloromycetin has been used in large doses, 16.5 gm. over seven days in chronic carriers but with no result.

INFANTILE GASTRO-ENTERITIS

Several methods of treatment for this condition are available including:

Pectin treatment—using a pectin-agar-dextre-maltose combination, grated apple or mashed banana.

Sulphonamides. Sulphaguanidine or succinyl-sulphathiazole may be given: absorption of these drugs is limited; therefore toxic effects are unlikely.

Antibiotics. Good results have been obtained especially in resistant cases with chloromycetin.

Parenteral administration of salines. Probably the most important complications of severe gastro-enteritis, particularly in young children, are dehydration and acidosis. These involve serious depletion in potassium ions with resultant symptoms including transient paralyses, cardiac enlargement and cardiac failure. It is necessary therefore that the deficiency should be replaced by parenteral solutions containing potassium such as KCl 2.7 gm. per litre, NaCl 4.4 gm. per litre, $NaHCO_3$ 4.0 gm. per litre.

This may be given intravenously suitably diluted 1 : 2 or 1 : 3 with 5% glucose solution, or may be given subcutaneously. Darrow recommends that 0.26 gm/Kg. of potassium chloride is a safe dose used with proper precautions to avoid an excessive increase in serum potassium level with the possibility of heart block. The safe dose of potassium and adequate amounts of sodium salts are contained in 80 c.c. of the above solution. It is desirable that dehydration should be treated with physiological saline with glucose.

In the subsequent treatment, i.e. during convalescence, a slow return to normal diet is desirable, otherwise relapse is likely to occur.

PEPTIC ULCER

The etiology of peptic ulcer is still a matter for much controversy, likewise the treatment.

It is generally accepted that internal and external environmental factors play a considerable part in the etiology of the condition and may cause considerable psychological trauma, especially in persons with certain characteristic personality patterns. Such trauma may precipitate marked physiological imbalance affecting mainly the upper alimentary tract.

In a recent article Freed discusses the effects of emotional stress on gastric secretion and mobility: he points out that fear diminishes gastric activity while anxiety causes marked hyperactivity. He has studied the relationship of various factors such as age, sex, race, etc., to the incidence of peptic ulcer over the past 50 years. His investigations show a definite sex and age shift during the period, resulting in an earlier age incidence and greater preponderance of the condition, especially duodenal ulcer, among males. Freed suggests that this may be due to a greater degree of social security now existing for females.

In regard to race incidence of peptic ulcer Freed points out that under normal conditions the condition is uncommon in the African, but in times of social upheaval such as war the Negro is more sensitive and the incidence increases considerably.

Factors of occupation, and economic position are important in that the incidence of peptic ulcer is higher in those engaged in employment or professions causing tension and nervous strain. The incidence is higher in urban than in rural populations, and the mortality rate increases in the lower income groups.

Much consideration has been given to food and digestion in relation to development of gastric and duodenal ulcer; opinions are divided. It is generally agreed that alcohol and tobacco and possibly caffeine are important in this respect. Discussing the physiological process of digestion in relation to the etiology of peptic ulcer, du Preez suggests that insufficient mastication may cause disturbance of normal gastric function to the extent that '90% of all hyperacidity must be sought in defective oral function'. Further he regards the habit of drinking with or immediately after meals as non-physiological and conducive to increase of gastric secretion to a final continuously hypersecreting state which in the end becomes pathological.

Pathogensis of peptic ulcer is still undecided. Following careful investigations, Deelman was unable to demonstrate any inflammatory change, infarction or embolism at the side of the lesions. He observed the presence of cracks or fissures in the mucosa extending to the muscular layer, which, he suggests, may be due to abnormality in tone and contraction of the musculature with ultimate degeneration of the mucosa in certain areas. This is characterized by replacement of epithelial tissue and glands by connective tissue which is stretched by contraction and relaxation of the musculature, deepening the fissure and finally causing ulceration. Multiple ulcers may arise in this way and it is therefore possible that exacerbations in duodenal ulcer cases may be due to formation of new ulcers.

The part played in the etiology of peptic ulcer by gastric secretion is controversial, especially in view of recent investigations. In many cases of peptic ulcer there is no change in gastric secretion during attacks and remissions. Examination of samples of gastric juice collected half-hourly day and night shows that in duodenal ulcer, day and night secretions are markedly acid. In gastric ulcer, day secretion may be of normal acidity while night secretion may be deficient in amount and in acidity. There is, however, no recorded instance of peptic ulcer with achlorhydria.

This suggests that the mechanism of formation of peptic ulcer does not follow an invariable pattern. Duodenal ulceration is generally associated with gastric secretion of large volume and high acidity: this may be due to a pathological process already present in the duodenum before onset of ulceration and accompanied by disturbance of physiological activity.

Treatment of Peptic Ulcer. Many and varied treatments have been introduced and it is now generally accepted that the basic principles are:

1. Physical rest.
2. Mental rest—promoted by sedatives, e.g. phenobarbitone, which is particularly valuable in the early stages of treatment.
3. Diet—designed to rehabilitate and to maintain the patient's condition to allow of maximum economic function.
4. Antacid and Antipeptic therapy.
5. Psychotherapy, since full co-operation by the patient is essential for successful treatment.

The aspects for consideration herein are diet briefly, and drug therapy, the main object of which is the buffering of gastric acidity below the level of pepsin activity but without neutralizing the acid completely.

Diet Therapy. This requires a diet of high protein, moderate fat and low carbohydrate content and of sufficient calorie value. This allows of considerable freedom from diet restriction with improvement of morale and of physical condition. Milk and eggs form an important part especially at the beginning of treatment. Protein hydrolysates are not, in general, acceptable as efficient buffering agents.

Drug Therapy, i.e. Antacid and Antipeptic Therapy. The desirable level of pH of gastric contents in peptic ulcer is between pH 2.0 and pH 4.0, i.e. pH 2.0 when there is no active ulceration and pH 4.0 during exacerbations of the condition. Antacid agents cause reduction of pH values to a variable extent and the rate of neutralization also varies.

1. *Effect on pH.* Maximum, i.e. definitely alkalinizing: Sodium bicarbonate, Magnesium oxide, Basic Magnesium Trisilicate.

Moderate effect: Magnesium Trisilicate, Calcium carbonate, Magnesium phosphate.

Minimal effect: Calcium phosphate, Aluminium hydroxide.

2. *Inactivation of Pepsin.* (a) Pepsin is very sensitive to the presence of aluminium salts especially between pH 1.0 and pH 3.7: therefore, with aluminium hydroxide and phosphate, inactivation is complete and persistent and aluminium chloride is formed. As this latter substance is a precipitating agent it may be undesirable when there is no active ulceration.

(b) During remission periods it may be desirable to administer Kaolin or Silicates which will absorb the pepsin but allow some proteolytic activity.

(c) Pepsin may combine with certain antacid agents to form insoluble complexes devoid of proteolytic activity, e.g. with magnesium trisilicates and antacid absorbents such as 'activated phosphates'.

Activated phosphates are complex combinations of hydrated silica with tribasic phosphates. They are prepared by simul-

taneous precipitation giving combinations such as: 25% silica with 75% calcium phosphate, 25% silica with 75% magnesium phosphate, 25% silica with 50% calcium phosphate and 25% magnesium phosphate.

The preparations are insoluble in water; with hydrochloric acid they form chlorides, phosphate and silica.

The action is combined antacid due to the PO_4 content and absorption due to the silica but this is greater in the complex compound.

OTHER METHODS OF TREATMENT

(a) *Administration of Fresh Cabbage Juice.* This is based on the theory that fresh cabbage juice contains an unidentified anti-peptic ulcer factor (vitamin U) which has specific healing properties in peptic ulcer. The factor is thermolabile so the cabbage juice must be used in a fresh state together with milk and raw eggs. The patient is required to take at least 1 litre of cabbage juice daily. Concurrent therapy is allowed for relief of pain, i.e. sodium bicarbonate, codeine and mild sedatives.

(b) *Anion Exchange Resin.* This complex synthetic resin has been administered in a short series of peptic ulcer cases with good results in 80%. The dose is 0.5-1.0 gm. orally every 2-4 hours, and the preparation is non-toxic even when given over a long period.

(c) *Enterogastrone.* This substance is regarded as the hormone present in duodenal mucosa which depresses gastric secretion, acidity and motility. It is available for therapeutic use but gives variable results in peptic ulcerations. Maximum effects are obtained with duodenal ulcer cases.

(d) *Methonium Compounds.* These were originally introduced as muscle relaxants to replace curare. The Hexamethonium compound 'C_6' has been found to inhibit gastric secretion of hydrochloric acid to the extent of achlorhydria also gastric motility for a long period. Twelve-hour night secretion of gastric juice was reduced in volume and acidity in ten duodenal ulcer cases.

In view of these effects and the low toxicity of 'C_6' it may be of value in treatment of duodenal ulcer. Administration is by the intramuscular route.

(e) *Vagotomy.* A series of more than 200 cases have been treated by Orr and Johnson for peptic ulcer by complete section of the vagi. The results after five years indicate that in carefully selected cases good results may be obtained, and further operative treatment may be carried out if required, e.g. gastro-enterostomy.

The treatment can be relied upon to reduce spontaneous gastric secretion and diminish acid response.

Vagatomy is not in itself a dangerous proceeding and side effects, complications, etc., are mild.

Side Effects. Relief of constipation; gain in weight.

Complications. Flatulence and colic; weakness; excessive sweating; tendency of hypoglycemia.

These generally subside within a few months of operation.

CARDIAC FAILURE

Cardiac failure has been classified in various ways, the two most generally used being:

A. *Division into three types*:

1. Congestive cardiac failure, characterized by peripheral oedema, hepatic and venous engorgement.
2. Dyspnoeic failure, characterized by predominant respiratory distress.
3. Anginal failure associated with pain of continued type (coronary thrombosis) or recurrent type (angina).

These overlap considerably since, e.g. dyspnoea may occur in the congestive type, and oedema is frequently seen in the dyspnoeic failure cases.

B. *Division in two types depending upon the state of cardiac output*:

1. '*Low output failure*' in which cardiac output is impaired. This occurs in: (a) hypertension, (b) valvular disease, (c) cardiac ischemia.

'*High output failure*' occurring in conditions which require an increase in cardiac output:

1. Anaemia
2. Emphysema } O_2 carrying power of the blood is reduced.
3. Metabolic conditions, e.g. vitamin B_1 deficiency.
4. Mechanical overloading, e.g. arterio-venous aneurysms.

Treatment of Cardiac Failure. The drug of choice is generally digitalis.

The Action of Digitalis. The site and mechanism of action of the Digitalis glucosides are still matters of controversy. The following have been suggested, i.e. that the improvement produced in congestive cardiac failure by digitalis bodies is due to:

1. Slowing of the rate, i.e. primary vagal stimulation. It should be noted that slowing is not invariable and marked clinical improvement may occur without reduction in heart rate.
2. Myocardial stimulation.
3. Reduction of venomotor tone (McMichael). In regard to the last theory, McMichael suggested that venous filling is the primary regulating mechanism for cardiac output, and from his experimental observations, concluded that the relief afforded by digitalis in 'low output failure' is due to reduction of venomotor tone and fall in venous pressure with secondary effects on cardiac output. Ouabain does not produce a marked fall in venous pressure so McMichael concludes that the action of ouabain is direct upon the myocardium.

The majority of cardialogists are, however, of the opinion that the action of both drugs is directly upon the myocardium. The heart muscle absorbs more digitalis bodies per gram than any other organ and these may be broken down at different rates accounting for the difference in speed of action, e.g. of digitalis and ouabain.

It has been suggested that the actual effects on the cardiac muscle are due to a 'cortin-like' action, i.e. retention of potassium within the muscle cell with improvement in all hydration.

Indications for Digitalis. Digitalis is definitely of value in:—

1. Congestive cardiac failure:
(a) With hypertension;
(b) With arteriosclerosis;
(c) With auricular fibrillation.

N.B.—Digitalis does not cure the fibrillation but partially blocks transmission of impulses via the A.V. conduction system and slows the venticular rate.

2. Occasionally of value in:—
Congestive cardiac failure:
(a) With heart block;
(b) With coronary thrombosis.

N.B.-Rapid digitalization in these cases is not desirable.

3. Paroxysmal tachycardia.

4. No effects may occur in:—
Cardiovascular syphilis;
Toxic myocarditis;
Myxoedema;
Hyperthyroidism;
Thiamine deficiency.

Digitalis is of no value in:—
Cardiac failure with shock;
Cardiac failure with cardiac compression;
Cardiac failure with pericardial adhesions;
Peripheral circulatory collapse in acute infective conditions;
Angina without cardiac failure.

Care should be exercised in giving digitalis to children with 'rheumatic hearts'. There is frequently a lack of response which might lead to increase of dosage to toxic levels. The lack of response is mainly due to active carditis.

Choice of Preparation. This may lie between a digitalis preparation, e.g. digitalis leaf and a digitalis glucoside, e.g. digitoxin.

Digitoxin ($C_{41}H_{64}O_{13}$) has been isolated in fairly pure form and may be given orally or intravenously. It is completely absorbed from the gastro-intestinal tract.

It is standardized biologically so that 0.42 mg. digitoxin = 1 cat unit of digitalis.

It is useful to note that 1.25 mg. digitoxin will produce the same extent of effect on ventricular rate, i.e. reduction, as 1.25 gm. digitalis leaf.

The action of digitoxin is the same as that of digitalis, only more persistent. The drug may be used for initial digitalization and for maintenance therapy by oral or intravenous route and the dose is the same for both routes.

Intravenously as Oral Administration. (a) *Initial Digitalization*:—

1.3-2.2 mg. over 3 to 6 days generally as 0.4 mg. six-hourly.
1.2-1.7 mg. as initial massive dose.

(b) *Maintenance Dosage*:—

0.1-0.2 mg. daily.

There is no relation to (a) body weight; (b) type or severity of cardiac failure.

Onset and Duration of Effects:—(a) *Oral.* Following oral administration effects are seen in 4-10 hours.

(b) *Intravenous effects* are produced in 25 minutes to two hours.

The maximum effects are seen in 4-9 hours and the duration may be two weeks. Regression of effect begins after two or three days.

Excretion is not constant; there appears to be an equilibrium between the amount present in the body and the rate of elimination; if this is limited then toxic effects occur and are more marked and more persistent than with digitalis.

Toxic Effects. These are the same as for digitalis, i.e. extensions of therapeutic effects. The onset may be expedited by indiscriminate use of mercurial diuretics.

In general, digitoxin produces rapid effects with small dosage compared with digitalis; it is, however, not desirable for routine digitalization in view of the persistent toxic effects.

The Significance of Salt Retention. Dock has pointed out that, in cardiac failure, methods of adaptation to reduction of venous return and diminution of myocardial force are numerous and effective for a period. In all cases there is:—

(a) A rise in venous pressure;
(b) A decrease in renal and splanchnic blood flow;
(c) A decrease of blood volume;
(d) An increase of extracellular fluid volume.

The predominance of (a) and (d) generally determines the type of failure, i.e.

With low output failure, the increase in extracellular fluid volume is marked but there may or may not be evidence of oedema. Increase of body weight occurs to the extent of 8 or 10 lb.

With high output failure the increase of venous pressure is the most marked symptom.

The primary cause of cardiac oedema may be disturbance of usual function, i.e. reduction of filtration rate due to reduced renal blood flow. Under such circumstances tubular reabsorption of sodium occurs with consequent increase in extracellular fluid volume. Compensation for the cardiac deficiency increases the ability to excrete sodium, but according to Briggs *et al.* compensated cases do not necessarily show a greater cardiac output than uncompensated cases; therefore renal circulation may still be inadequate and the oedema still present.

It would appear then that depletion of salt intake may be desirable in low output failure and incompensated cases where oedema is still present. This involves:

1. Restriction of salt intake;
2. Free fluid intake;
3. Mercurial diuretics.

The object of administration of mercurial diuretics is to increase further the sodium and chloride excretion which is a feature of the diuresis with mercurials. If mercurial diuretics are used then salt restriction need not be so severe.

The necessity for administration of digitalis in conjunction with the above treatment is a matter of controversy but in general the results of the combined therapy are more satisfactory.

Intractable cases with marked ascites may be associated with hypoproteinemia due frequently to deficient protein intake. A high protein diet is therefore indicated.

Acute pulmonary failure with marked dyspnoea and oedema, generally nocturnal in occurrence may be partly gravitational and neurogenic or reflex in origin; capillary dilatation and increased permeability occur with resultant fluid accumulation.

Treatment of such cases should include:—

1. Sedatives, e.g. morphine, barbiturates (intravenously if necessary);
2. Oxygen;
3. Theophylline ethylene diamine;
4. Adoption of the prone posture when at rest in preference to the supine, and raising the head of the bed. Such patients also benefit from the salt depletion regime and mercurial diuretics.

In cases of high output failure with high venous pressure, e.g. cardiac failure with emphysema, oxygen and mercurial diuretics are of value generally given with digitalis. It should be noted, however, that digitalis may reduce the venous pressure but cardiac output will also be reduced conceivably to a dangerously low level in some cases.

N.B.—In patients who are fully digitalized, the drug may be stored in oedema fluid, therefore care is essential in giving mercurial diuretics so that rapid diuresis may be avoided. Otherwise 'spontaneous redigitalization' may occur with resultant toxic effects.

Essential Hypertension. Opinions are divided regarding the treatment of essential hypertension. The primary considerations are:—

(a) Type of Hypertension, i.e.

1. Benign—generally occurring in older patients, of slow onset and frequently unnoticed.

2. Malignant—found in young patients, of rapid onset and produces serious results. A marked symptom is severe headache.

(b) Surgical *versus* Medical Treatment.

Surgical treatment involves sympathectomy or leucotomy with certain attendant disabilities.

Medical treatment necessitates the use of sympathetic agents, or some dietetic or other regime.

Benign Essential Hypertension. The results of surgical and/or medical treatment are unsatisfactory. A dietetic regime directed, if necessary, to reduction of body weight is desirable together with sedatives.

Malignant Essential Hypertension: *Surgical Treatment.* (1) *Sympathectomy.* This frequently gives good results with alleviation of symptoms especially headache, and possible prolongation of life. It should be remembered that sterility may follow the operative treatment in male patients.

(2) *'Chemical Sympathectomy.'* Debilitated patients with malignant hypertension and those over the age of 60 years cannot be submitted to open sympathectomy. It is, however, possible to block the paravertebral sympathetic chain by injection of 6 to 10% phenol in aqueous solution. Haxton reported a series of 200 cases in which he obtained good results with few complications.

(3) *Leucotomy.* Recently a case has been reported in which prefrontal leucotomy was performed in a case of hypertension associated with severe headaches and marked depression. Following the successful surgical treatment the mental symptoms subsided followed by anticipated personality changes. The important feature of the case is the stabilization of blood pressure between reasonable limits and relief of symptoms of hypertension, e.g. headache and utinal haemorrhage. It is suggested that prefrontal leucotomy might be considered as a last resource in chronic cases.

Medical Treatment. Excessive vascular tone which is primarily the cause of increased blood pressure may be due to one of several causes:—

(a) Increase of vasoconstrictor impulses from the vasomotor centre.
(b) Excessive reflex tone.
(c) Some change in the metabolism of the blood vessels.
(d) An abnormal constituent in the blood causing vasoconstriction.

Diminution of the vascular tone can be produced by:

A. Blocking of sympathetic ganglia.
B. Reducing of the nerve impulses to the blood vessels.

A. *Blocking of Sympathetic Ganglia.* The most satisfactory results have been obtained with quaternary ammonium bases.

Action. The quaternary ammonium bases have a wide range of pharmacological activity including:—

(a) A curare-like action on skeletal muscle.
(b) A stimulating action on the vagus causing cardiac slowing.
(c) A blocking action on autonomic ganglia and therefore inhibition of structures supplied by the autonomic nervous system.

The preparation commonly used is tetraethyl ammonium bromide ('Etamon'). This substance will produce diminution of peripheral vascular tone by depression of the sympathetic ganglia, and thereby a reduction of blood pressure from 10 to 20%. The effect is seen only in hypertension.

Etamon shows important side actions and toxic effects such as:—

(a) Dilatation of the pupil;

(b) Numbness of the periphery with feeling of intense cold;
(c) Curare-like effects;
(d) Depression of gastro-intestinal motility;
(e) Reduction of gastric secretion.

In view of the fact that all ganglia are affected by Etamon the drug should be used with caution.

C_5 and C_6. The most recent additions to the group of ganglian blocking agents are the methonium compounds 'C_5' and 'C_6'. These substances produce blocking of sympathetic ganglia and a marked fall in blood pressure with postural hypotension in hypertensive cases. This is accompanied by prolonged vasodilatation in the lower limbs, the upper limbs showing little effect; the action is 'greater and more constant than that of tetra ethylammonium' . . .

C_5 = pentamethonium iodide.
C_6 = hexamethonium iodide.

The compounds belong to the same series as C_{10}—decamethonium iodide, a muscle relaxant for which C_5 is the antidote.

The action of C_5 and C_6 if excessive can be antagonized by adrenaline as ephedrine.

With reference to the site of action of C_5, it has been shown C_5 does not prevent the peripheral action of adrenaline, and further that the drug causes vasodilatation in a sympathectonized limb, suggesting that the action may be directly on the blood vessels.

B. *Depression of Nerve Impulses to the Blood Vessels.* This can be attained with the use of adrenergic blocking agents. This group of substances includes:

Ergot alkaloids, e.g. Ergotamine.
Dihydroergotamine.
Dibenamine.
Dioxane derivatives, i.e. F.933 and F.1164.
Priscol.
Yohimbine.
Corynanthine.

Dibenamine. As a therapeutic agent the most satisfactory substance is Dibenamine. This drug produces a gradual fall of blood pressure reaching a maximum activity within 24 hours and this effect may last for several days.

Administration is by the intravenous route, the dose 4-6 mg./Kg.

Dibenamine has been used for peripheral vascular disease and in hypertension: in the latter condition a preliminary transient orthostatic hypotension may occur.

Dioxane derivatives. F.933 has been used as a diagnostic agent in hypertension associated with the occurrence of a phaeochromocytoma: this adreno-medullary tumour contains large amounts of adrenaline which may cause persistent vasoconstriction and high blood pressure. The administration of F.933 in these cases is followed by a marked fall in blood pressure due to 'neutralization' of the adrenaline.

The adrenergic blocking agents may be of value in cases where hypertension is associated with renal ischaemia. In this condition pressor amines have been shown to form in the kidney probably from dihydroxy-phenyloxyalamine, and these have similar vasocoustuclar effects to adrenaline and may be 'neutralized' by one of the adreyergic blocking agents.

Further renal ischemia may be a factor in inactivation of amine oxidases which normally destroy adrenaline and the pressor amines.

Recent theories suggest that renal ischemia is not essential for hypertension and therefore formation of the pressor amines noted previously and of augiotomin may be seen only in a few hypertensive cases.

Rice Diet in Hypertension. The introduction of this treatment is based upon the theory that in hypertension the kidney is unable to excrete protein breakdown products, therefore a diet containing the minimum amount of protein should be given. The necessity for this is not proven but the treatment is safe. It is possible that relief of hypertension in some cases is due to the low salt content of the diet, i.e. to sodium depletion.

The diet consists of rice, sugar and fruit with added vitamins and iron to give 2,000 cals., i.e.

460 gm. carbohydrate.
5 gm. fat.
20 gm. protein.
160 mg. salt.

Equally good results were obtained with inclusion of 70 gm. of protein and 200 mg. of salt.

Ayman suggests that the chief value of this treatment is psychological: loss of body weight may be of contributory value.

Use of Anticoagulants and Antibiotics. The value of anticoagulants is shown mainly in:—

(a) Coronary thrombosis.
(b) Pulmonary embolism.
(c) Subacute bacterial endocarditis.

In Coronary Thrombosis. Frequency of thromboembolism is diminished and the mortality rate from this has been much reduced by giving anticoagulants (24% 15%).

Treatment aims at reduction of prothrombin to 20% of the normal level and maintenance for three weeks.

The Mayo Clinic method using Dicoumarol is generally satisfactory.

300 mg. Dicoumarol—1st day.
200 mg. Dicoumarol—2nd day.
50-200 mg. Dicoumarol—maintenance therapy.

Repeated prothrombin estimations are essential. In severe cases 50 mg. Heparin intravenously 4-hourly may be given concurrently for 2-3 days. Similar treatment may be used for Pulmonary embolism.

Sub-acute Bacterial Endocarditis. Penicillin with or without:
(a) Caronamide;
(b) Anticoagulants
may be effective. The dose of penicillin required is high—2×10^6 units daily with high protein diet.

Syphilitic Aortic Disease. Good results have been obtained especially in patients under 50 years with massive doses of Penicillin (8 or 12×10^6 units daily) over a period of eight to 10 days. This should be preceded by a course of Bismuth and Potassium iodide medication for 2-3 months.

Thyroid Heart Disease: Hyperthyroidism. Tachycardia, etc., may respond to thiouracil.

Thiouracil and allied compounds may be of value for reduction of the B.M.R. in cases of cardiac failure without hyperthyradism.

Hypothyroidism. Cardiac complications are rare but generally respond to thyroid medication.

Khellin. This substance is the active principle of the seeds of *Ammi visnaga*, a plant used as an antipasmodic in colic in the Near East. Chemically Khellin is related to Coumarin.

Action. Khellin is a powerful dilator of smooth muscle including that of the coronary blood vessels and the bronchi. No action is produced on the myocardium or on blood pressure. The effects are somewhat slower than those of nitroglycerin, but prolonged up to 36 hours.

The drug may be administered orally or for more rapid action by the intra-muscular route.

No toxic effects or tolerance to the drug have been observed.

Relief of symptoms in 83% of cases of angina pectoris has been reported with initial doses. 100 mg. once or twice daily followed by 50 mg. three times daily by mouth. Good results have also been obtained in asthma; larger doses are required but the single dose (200-300 mg.) intramuscularly may give immediate and lasting relief.

Khellinin and Visnammin which are also found in the plant produce definite effects on the myocardium in experimental animals. Khellinin increases myocardial contractility and cardiac output with no vaso-constrictor action. Visnammin reduces the contractility and diminishes output. Both drugs act as coronary vasodilators.

ACTH, CORTISONE AND ALLIED STERONES

Kendall and his associates have isolated a number of sterones from the suprarenal cartex which exert a variety of effects upon metabolism. These include:—

1. Regulation of electrolyte balance.
2. Regulation of carbohydrate, protein and fat balance.
3. Androgenic or anabolic effects.

The steroid compounds so far isolated include

11—corticosterone. } These exert the most powerful
11—desoxycorticosterone. } effect upon electrolyte balance.
11—oxysteroids. { Compound A. / Compound B.
11—desoxcortisone. { Compound E. / Compound F. } = Cortisone.
11-17—oxysteroids.

The chief actions of the oxysteroids are an carbohydrate metabolism: Compound E and Compound F also show marked effects on lymphoid tissue and circulating cosinophils. The androgenic group of steroids is concerned with masculinization and retention of nitrogen and phosphorus.

RELATIONSHIP BETWEEN ADRENAL STEROIDS AND RHEUMATOID ARTHRITIS

Sterone Deficiency Theory: Hench has suggested that rheumatoid arthritis and other similar diseases may be regarded as due to a deficiency of bisexual hormone, possibly a sterone of adrenocortical origin. This is based upon the fact that if pregnancy or jaundice occur in a case of rheumatoid arthritis a temporary remission of symptoms may result. Disturbance of sterol metabolism is a characteristic finding in both conditions.

Adaptation Syndrome. Selye has shown experimentally that exposure of animals to sudden stress, e.g. cold, acute infections, etc., produce a state of shock, the degree of which varies according to the extent and period of stimulation. He divides the effects into three stages:

1. 'Stage of alarm' produced by sudden severe shock.
2. 'Stage of adaptation' produced by repeated sub-lethal stimuli to which the animal becomes accustomed but shows abnormal sensitivity to other stimuli of similar nature.
3. 'Stage of exhaustion' produced by continual stimuli over a long period and terminating in death.

During the stage of adaptation the adrenal cortex undergoes hypertrophy. Selye and his associates found that a similar hypertrophy occurs with simultaneous 'adaptation reactions' following administration of crude adrenocorticotropic hormone from the anterior pituitary.

Further, overdosage of animals with Desoxycorticosterone or with the naturally occurring hormone, Desoxocortisone produces essentially the same changes as the 'adaptation syndrome', more readily in adrenalectomized animals. It has also been shown that these substances reduce the resistance of the tissues to traumatic shock. In this latter connection it should be noted that Corticosterone and cortisone increase this resistance, i.e. these sterones and their reduction products are antagonistic.

The reactions characterizing the 'adaptation syndrome' closely simulate various hypertensive, allergic and rheumatic conditions in man, including rheumatoid arthritis. Such conditions in many may follow exposure to cold, acute infective conditions, etc. Selye and Pentz therefore suggest that these diseases are 'caused by an abnormal (probably excessive) adaptive response of the adrenal cortex and represent diseases of adaptation'.

Recently Selye has shown that administration of Desoxocortisone to animals produces extensive hyalinosis of tissues similar to the condition obtaining in the so-called 'collagen diseases'; these may therefore be manifestations of the adaptation syndrome. It has been suggested that they are essentially hypersensitivity reactions.

The foregoing suggests that endocrine and biochemical imbalance may be important factors in the etiology of rheumatoid arthritis, etc., and further that the endocrine factor is the supprarenal. Thorn and Bayliss were unable to find any adrenal dysfunction in 18 out of 21 rheumatoid arthritis cases. Marrian and his colleagues, however, found that abnormalities of steroid metabolism, i.e. of progesterone, actually occur in rheumatoid arthritis. This may also account for the remissions in the disease observed during pregnancy.

Use of Cortisone, etc., in Rheumatoid Arthritis: 1. *Cortisone.* In support of their theory of the causation of rheumatoid arthritis and in an attempt to reverse the physiological disturbances associated with it, Hench and his co-workers administered the 11-17-oxysteroid, Compound E or Cortisone to a small series of cases with dramatic results. There was an immediate remission of symptoms, disappearance of stiffness and immobility with general improvement in health and well-being. These effects continued during the period of administration of the drug, but subsided on cessation with a return of the arthritic state.

The treatment was extended to arthritis associated with other diseases, e.g. lupus erythematosus, psoriasis, etc., and gout and to a small number of cases of rheumatic fever with equally good results.

2. *ACTH.* Since the function of the adrenocorticotropic hormone (ACTH) is to stimulate secretion of adrenocortical hormones, then administration of this hormone may be beneficial in rheumatoid arthritis, etc., provided the suprarenals are functioning adequately. Definite increase in adrenal cortex hormone secretion has been found following ACTH administration.

ACTH has been used with equal advantage in the conditions which respond to Cortisone. This finding bears out the statement that the 11-17 oxysteroids are present in the greatest proportion in the natural adrenal cortex secretion. Compound F is said to predominate.

3. *Desoxycorticosterone with Ascorbic Acid.* Desoxycorticosterone has presumably no cortisone activity, and is probably actually antagonistic to the 11-17-oxysteroids.

Lewin and Wassen found that if the injection (IM) of desoxycorticosterone is followed after five minutes by intravenous injection of ascorbic acid, the relief of symptoms of rheumatoid arthritis is equally satisfactory. These results have in general been confirmed by other workers, including Le Voy and Laxton in a series of 80 cases.

Recently an attempt has been made to explain the action of the combined drugs. Ascorbic acid may produce slight relief of symptoms of rheumatoid arthritis: similar effects are observed after injection of Methylene blue which is an oxidizing agent. Full beneficial effects are obtained by giving desoxycorticosterone in both instances. This suggests that the methylene blue and probably the ascorbic acid oxidise the desoxycorticosterone.

The importance of these findings lies in the fact that desoxycorticosterone may be obtained synthetically and is therefore cheaper and more easily available. Further, the dose is less and the action apparently more rapid.

Uses of Cortisone, etc. Following on the results obtained in rheumatoid arthritis the use of cortisone, etc., has been extended to the treatment of a variety of other diseases:

Gout.
Psoriasis.
Lupus erythematosus.
Ankylosing spondylitis.
Hodgkin's disease.
Various allergic conditions including hay fever, urticaria, dermatitis exfoliation.

Many of the above conditions fall into the category of 'Collagen diseases', which it has been noted may be hypersensitivity reactions. Further, these diseases have a common characteristic of cosiniphilia and the adrenal steroids especially the 11-17-oxysteroids produce marked reduction in circulating cosinophils.

Mechanism of Action of Cortisone, etc. This is not yet known. One theory suggests that the adrenocortical sterones block hypersensitivity reactions in the tissues. This is supported by the fact that the sterones are known to have antihistomine properties.

The action of the corticosterones appears to be a general one on connective tissue and the manifestations may be the result of alteration of reactivity to trauma. The drugs also show antihyaluronidase activity.

Complications of Therapy: *Mild.* Water retention with gain in body weight. Increase in blood pressure. Mild cerebral stimulation.

Severe. Potassium deficiency symptoms. A mild degree of Cushings syndrome. Encephalapathy.

These generally disappear on withdrawal of the drug but caution in use is necessary.

Other Substances with 'Cortisone Activity': ACTP. Morris and Morris have recently isolated a polypeptide, ACTP, from pituitary gland extracts. This preparation has 10 times the activity of the protein hormone prepared by Lang *et al.* Similar polpeptides have been obtained by C.H. Li.

Other Sterols. Several sterols have been found to show Cortisone activity including Testosterone. Opinions are divided regarding the activity of Progesterone.

A recent investigation shows that certain plant sterols have ACTH activity or may be used as sources of synthetic Cortisone. Chief among these are saprogenins, i.e. 'Aristone' related to pregneninolene and the sterol found in *Strophanthus sarmentosus* which may serve as a basis for preparation of cortisone.

Careful examination of cases of the therapeutic value of cortisone and similar substances is essential: the therapy is

very recent and in such conditions as rheumatoid arthritis a long term view must be taken. The duration of treatment is also a matter for consideration as it appears that the treatment may be necessary throughout the patient's life. Further, there are dangers attendant upon indiscriminate medication.

DOSAGE OF CORTISONE, ETC.

Cortisone ...	300 mg. IM. initial dose. 100 mg. IM. (75 mg. may be sufficient in some cases.)
ACTH ...	40 mg. IM.
Desorycorticosterone Ascorbic Acid	0.5 mg. IM. followed after five minutes by 1.0 gm. ascorbic acid intravenously.

NEW PREPARATIONS AND APPLIANCES

'STOLIC' FORTE IN THE TREATMENT OF HYPERTENSION

Hypertension is a commonly encountered condition in medical practice, and statistics indicate that approximately 85% of hypertensive cases are of the essential or idiopathic type.

For the treatment of essential hypertension, the Medical Research Division of Sharp & Dohme has developed *Stolic Forte*:

Mannitol hexanitrate	30 mg.	per tablet
Rutin	20 mg.	
'Delvinal' vinbarbital sodium	30 mg.	

Stolic Forte eliminates the necessity for administering two different medicaments by serving the dual purpose of providing prolonged vasodilation and effective sedation.

Mannitol hexanitrate, slowly exerts its vasodilating action on the smooth muscle fibres of the arterial system and consequently vasodilation is prolonged. For this reason Mannitol hexanitrate is more effective than amyl nitrite and sodium nitrite which exert a very rapid vasodilator action and are of little value except in certain cases where an immediate effect is desired.

Clinical evidence indicates that following the administration of Mannitol the blood pressure begins to fall within 15 to 30 minutes and reaches the maximal decrease in 2½-3 hours.

The extent of the decrease in systolic pressure is approximately 35 mm. Hg and the duration of action is from four to six hours.

Stolic Forte includes in its formula the drug Rutin, well known for its effect in decreasing the abnormal capillary fragility that may be associated with hypertension.

Stolic Forte also contains *Delvinal vinbarbital sodium*, noted for its sedative action in allaying apprehension and levelling off the emotional fluctuations of blood pressure.

Delvinal is characterized clinically by its moderate duration of action and the fact that the patient experiences little sensation of drugging throughout the period during which the drug is taken.

The suggested adult dosage of *Stolic Forte* is from one to two tablets at intervals of from four to six hours.

In those instances where the systolic pressure is excessively elevated, the dosage may be increased in accordance with clinical judgment.

Stolic Forte is supplied in bottles of 100 tablets.

VERENIGINGSNUUS : ASSOCIATION NEWS

BARAGWANATH HOSPITAL MEDICAL SOCIETY
AUGUST MEETING

Dr. Vernon H. Wilson read a paper on *Oxygen Administration*. The paper was presented in an attempt to rationalize oxygen administration and re-examine by blood oxygen saturation estimation, the value of nasal catheter methods of administration.

The nursing staff and junior members of the medical staff, who are personally responsible for the maintenance of continuous oxygen administration, find the oxygen tent and B.L.B. mask difficult to apply in European and non-European medical practice. The tent is expensive, easily damaged, often frightening to the patient who cannot hear or make himself heard, humid and hot even when attention is directed to the cooling system. The B.L.B. mask gives a sense of resistance to breathing, is heavy and uncomfortable and often fits the nose imperfectly. In consequence, apart from helpless patients, these methods are seldom tolerated for long periods so that the patient forces his way out of the tent and throws off the B.L.B. mask. Further, even when these methods are tolerated the patient often dies in spite of every care and attention.

Having observed several ambulatory patients over many months with moderately severe anoxaemia, secondary to generalized respiratory diseases, Dr. Wilson questioned if oxygen was the vital therapeutic agent we believed. As an example he quoted one patient with advanced emphysema who was able, as an out-patient, to walk briskly with him around the hospital with femoral arterial oxygen and venous saturations of 52% and 20% respectively.

Over 600 estimations had been performed by the Haldane method as described by Douglas and Priestly in *Human Physiology*. The method was considered entirely satisfactory, the mean error on identical samples from 10 patients being 1.6%, the range being from 0 to 4%. This degree of accuracy agreed with the work of Courtice and Douglas who compared the van Slyke with the Haldane method, using various buffer solutions. It was observed that both femoral arterial and venous samples had been simultaneously estimated to avoid confusion in Dr. Wilson's work.

Dr. Wilson then showed that oxygen was not likely to benefit patients with cardio-vascular failure without respiratory disease. He presented oxygen saturation estimations upon 12 patients with various diseases. Even moribund cases showed femoral arterial and venous figures above 70% and 20% respectively with cardio-vascular failure.

With generalized respiratory disease, however, systemic blood oxygen saturation estimation showed that oxygen might be beneficial. Dr. Wilson showed figures from 12 patients with cor pulmonale to illustrate figures of 40% to 60% femoral arterial oxygen saturation. He noted, however, that even at their worst periods these patients had not been anoxic, as a considerable amount of oxygen was still present in the blood returning to the heart, and that most of them recovered without oxygen administration as shown by serial blood oxygen estimations.

In 15 patients the femoral venous oxygen saturations had been compared with the saturation of the blood taken from the heart chambers and was shown to be similar. Further, Dr. Wilson showed how all the oxygen could be dissociated from the blood after exercising the legs in severe anaemia and in anoxaemic patients with cor pulmonale secondary to generalized respiratory disease.

Serial oxygen saturation estimation upon samples from the femoral artery and vein before and during oxygen administration in two patients, showed how the femoral venous oxygen figures rose parallel with the arterial oxygen saturation.

These observations would suggest that even severely anoxaemic patients had sufficient oxygen for their requirements and agree with clinical experience that chronic anoxaemia was seldom associated with symptoms and signs of anoxia.

The work of Bing and his co-workers showed that the oxygen content of the coronary sinus blood was considerably lower than the content of blood in the heart chambers; and Motley and Cournand had shown that pulmonary artery pressure rises when the oxygen content of the inspired air was reduced.

Dr. Wilson then produced evidence that oxygen administration with Tudor Edwards spectacles was highly effective in 14 patients, upon whom serial estimations had been performed, before and during oxygen therapy after 15 minutes at 2 litres per minute. This method of administration was economical, comfortable and tolerated continuously for days and nights if necessary; and effective even if the patient was breathing through the mouth.

The purpose of the paper was to show that an easy and economical method was as effective as the complicated and expensive and that oxygen administration was not always a vital therapeutic measure.

PASSING EVENTS

We regret to record the death of Dr. Richard Kammer of Durban.

* * * *

We regret to record the sudden death of Sir Ernest Graham-Little, M.D., F.R.C.P. in his 84th year, at his Epsom home. Sir Ernest's mother came from Cape Town and he himself was educated at the South African College, where he took his B.A. degree and a gold medal before proceeding to London to study medicine at Guy's and St. George's Hospitals.

* * * *

Dr. H. S. Gear, a member of Federal Council of the Medical Association of South Africa, has returned from meetings of the World Health Organization in Geneva. Dr. Gear is Chairman of the Executive Board of the World Health Organization and a member of the International Expert Committee on Epidemiology and Quarantine.

* * * *

Dr. Allan V. Bird and Dr. Andrew C. Watt have entered into partnership as neurologists at 404 Medical Centre, Jeppe Street, Johannesburg. Telephone: 22-7275.

THE CAPE TOWN PAEDIATRIC GROUP

A meeting will be held in the Little Lecture Theatre, Groote Schuur Hospital, on Monday, 27 November 1950 at 8.15 p.m.

Dr. I. Mirvish will give his Presidential Address on *Reflections on the Sixth World Paediatric Congress at Zurich.*

* * * *

Copies of the bi-monthly Medical and Surgical Newsletters, issued by the United States Information Service, can be obtained on application to the Information Officer (Mr. B. A. Thirkield), United States Information Service, American Consulate-General, 23 Beckett's Building, President Street, Johannesburg.

A PRIMARY FELLOWSHIP EXAMINATION IN SOUTH AFRICA

The Royal College of Surgeons of England is prepared to conduct an examination in South Africa for the 'Primary Fellowship'.

If the numbers reach the minimum of 50 entrants, as required by the R. C. S. England, the Association of Surgeons of South Africa will endeavour to arrange for the examination.

The entrance fee is £40 (sterling). Those interested should communicate with Dr. W. Kark, Honorary Secretary, The Association of Surgeons of South Africa, Medical House, 5 Esselen Street, Hospital Hill, Johannesburg.

* * * *

Dr. Ryno J. V. Milner, M.B., Ch.B. (Cape), F.R.C.S. (Edin.), has joined Drs. Wykerd and Roux as a specialist Ear, Nose and Throat Surgeon at Southern Life Building, 101 St. George's Street, Cape Town. Telephones:—Rooms: 2-1938; Residence: 4-1101.

BARAGWANATH MEDICAL SOCIETY

The next meeting will be held in the Nurses' Training School on Monday 27 November 1950 at 8 p.m. Mr. L. Fatti will lecture on the *Surgery of Congenital Heart Disease.*

* * * *

Dr. Wolf Rabkin and Miss Maria Olivier were married in Johannesburg on 7 November.

* * * *

To Dr. and Mrs. David Barron (*nee* Mavis Tobias) a daughter, on 7 November, in Cape Town.

IN MEMORIAM

DR. R. D. PARKER, *O.B.E.*

By the death of Dr. R. D. Parker the profession has lost one of the best type of general practitioners.

Parker graduated at Cambridge in the late nineties. He served in two wars, the Anglo-Boer and the Great War. For many years he practised at Caledon. His popularity and the soundness of his medical abilities will be remembered by many living at Caledon and in the surrounding districts. He retired from private practice in 1914. After spending five years with the S.A.M.C., he settled in Cape Town.

A man of culture, wit and artistic ability he was withall an English gentleman. He will be missed by his intimate friends.

Cape Town. L. G.
1 November 1950.

REVIEWS OF BOOKS

BRITISH SURGICAL PRACTICE

British Surgical Practice, Volume 7. **Edited by Sir Ernest Rock Carling, F.R.C.S., F.R.C.P. and Sir James Paterson Ross, *K.C.V.O.*, M.S., F.R.C.S. (Pp. 591 + xxvi. With 339 illustrations and four plates. 66s.) Butterworth & Company Limited, 1 Lincoln's Court, Masonic Grove, Durban. 1950.**

Contents: 1. Pharyngeal Diverticula. 2. Physiotherapy. 3. Physique, Body Build and Posture. 4. Pituitary Tumours. 5. Plastic Surgery—Corneal Grafting. 6. Pleura-Diseases of. 7. Poliomyelitis. 8. Polycystic Disease. 9. Post-Operative Gangrene. 10. Pregnancy—Surgical Intervention During. 11. Prostate. 12. Protracted Illness—Management and Rehabilitation. 13. Pulmonary Abscess. 14. Pulmonary Tuberculosis. 15. Pylephlebitis. 16. Pyloric Stenosis of Infants. 17. Rabies. 18. Radio-Active Isotopes. 19. Radiotherapy. 20. Reconstruction of the Ear and Nose. 21. Rectum—Benign Tumours of. 22. Rectum—Carcinoma of. 23. Rectum—Haemorrhoids. 24. Rectum—Proctitis. 25. Rectum—Prolapse. 26. Refrigeration Anaesthesia. 27. Resuscitation. 28. Retina. 29. Sacro-Coccygeal Region—Surgery. 30. Salivary Glands. 31. Scalp and Skull. 32. Schistosomiasis. 33. Sciatica. 34. Sclera. 35. Scurvy—Masked and Manifest. 36. Skin—Diseases of, in Relation to Surgery. 37. Speech Therapy. 38. Spinal Column. 39. Spinal Cord. Index to Volume 7.

The seventh volume of this work, like the previous volumes, deals with a large number of surgical subjects both general and specialized. The chapters on special subjects are written by experts and are excellent.

Morley deals with pharyngeal diverticula and gives an admirable account of the treatment. He recommends a transverse collar incision at the level of the cricoid cartilage.

Hawkins contributes a chapter on surgical intervention during pregnancy and deals with all the important surgical complications occurring in pregnancy.

Riches writes in a most comprehensive manner on diseases of the prostate and gives many useful hints derived from his extensive clinical experience. He includes a detailed description of Millin's retropubic prostatectomy.

Surgeons from the Brompton Hospital contribute very sound articles on the surgical aspects of pulmonary diseases and the chapter by Price Thomas on tuberculosis is particularly good.

Twistington Higgins gives an account of pyloric stenosis of infants. He divides the condition into three groups according to the duration and describes the pathological findings in each. The Ramstedt operation is described in detail and illustrated with excellent photographs.

Sir Harold Gillies and Patrick Clarkson deal with reconstruction of the ear and nose in an admirable manner and describe the various operations in a simple way.

The best articles are those on the rectum by various members of the staff of St. Mark's Hospital. Cuthbert Dukes writes on benign tumours giving a very concise account of a subject which is not very well known. Lloyd-Davies and Naunton Morgan contribute the chapter on carcinoma and discuss its operative treatment in detail including an excellent description of their synchronous combined method of excision of the rectum. Milligan contributes a masterpiece on haemorrhoids and his article should be carefully studied by anyone who has to deal with this common complaint. His description of haemorrhoidectomy is classical. Henry Thompson deals with prolapse and gives a well-illustrated account of the operation of rectosigmoidectomy.

Sol. Cohen contributes a useful article on refrigeration anaesthesia; Lambert Rogers writes on the surgery of the spinal cord; A. K. Henry gives an account of his vast experience of schistosmiasis; and in addition there are several other useful chapters on various subjects. In all of these a particularly high standard has been maintained, a feature which has been present throughout all the volumes of this great work.

NON-GONOCOCCAL URETHRITIS

Non-Gonococcal Urethritis. By. A. H. Harkness, M.R.C.S., L.R.C.P. (Pp. 424 + xii. With 167 illustrations, 73 in full colour. 52s. 6d.) Edinburgh: E. & S. Livingstone Limited.

Contents: 1. History of Non-Gonococcal Urethritis. 2. Residual Non-Gonococcal Urethritis or Post-Gonorrhoeal Urethritis. 3. Primary Bacterial Urethritis of Venereal Origin. 4. Bacterial Urethritis Due to Neisseria Other Than the Gonococcus. 5. Diphtheritic Urethritis. 6. Pasteurella Urethritis. 7. Differential Diagnosis of Primary Urethritis due to the Gonococcus and other Bacteria. 8. Spirochaetal Urethritis. 9. Desquamative Urethritis. 10. Diseases of the Genito-Urinary Tract due to the Virus of Inclusion Conjunctivitis and Pleuropneumonia-like Organisms. 11. Abacterial Urethritis (Aseptic Urethritis) of Venereal Origin. 12. Reiter's Disease. 13. Reiter's Disease—continued. Keratodermia Blennorrhagica. 14. Non-Gonococcall Infections of the Bulbo-Urethral Glands of Cowper. 15. Traumatic Urethritis. 16. Urethritis due to Local Diseases—Condylomata Acuminata (Venereal Warts). 17. Urethritis Descending from Stricture of Urethra and Infections of Cowper's Glands, Prostate, Vesiculae Seminales, Bladder, Ureters and Kidneys. 18. Protozoa, Metazoa and Fungi as Causes of Urethritis—Urethritis due to Protozoa. 19. Urethritis due to Focal Infection. 20. Urethritis due to Systemic Diseases—Septicaemia and Pyaemia. 21. Urethritis due to Metabolic and Deficiency Diseases. 22. Urethritis Ab Ingestis. 23. Non-Gonococcal Urethritis in the Female, Including Prolapse of the Urethra and a Distinctive Type of Traumatic Urethritis. 24. Non-Gonococcal Urethritis in Children. 25. Stricture of the Urethra with Non-Gonococcall Aetiology. 26. Conditions Simulating Non-Gonococcal Urethritis. 27. The Value of the Complement Fixation Test for Gonorrhoea in Differential Diagnosis. 28. Non-Gonococcal Paraurethritis. 29. Applied Anatomy—Urethral Mucous Membrane. 30. Special Types of Treatment—Sulphonamide and Antibiotic Therapy. 31. Criteria of Cure in Non-Gonococcal Urethritis.

Since the introduction of penicillin and the newer antibiotics the problem of treating gonorrhoea has diminished to manageable proportions. The alarming complications, seen so frequently in the old days, are now but rarities; but a minor problem now presents itself. All too frequently patients complain of a continuance of urethral discharge long after the time when experience shows they should be cured. Many patients, too, present themselves with a mild urethritis which repeated examinations shows to be non-gonococcal. This non-specific urethritis seems to be on the increase; and its challenge, although a minor one, constitutes a vexatious problem.

In a large volume of over 400 pages Dr. A. H. Harkness deals with this subject under the title of *Non-Gonococcal Urethritis*. Every known cause of urethritis is dealt with, bacterial, traumatic and urethritis caused by involvement of the urethra in general systemic diseases; it includes even that caused by a small fish which, we are told, has the disagreeable habit of plunging into the urethra of unwary bathers—fortunately only in the waters of the Amazon River and its tributaries!

Special interest centres round the account of urethral infections due to a virus similar to that found in inclusion conjunctivitis and in diseases such as lympho-granuloma and psittacosis. Dr. Harkness also writes of syndromes caused by an organism identical with that which causes pleuropneumonia in cattle. He gives a detailed description of such rare conditions such as Reiter's disease, Behcet's syndrome, etc., all of which he believes are caused by a filterable virus, revealed in smears after 24 hours' treatment with Giemsa's stain. Many beautifully coloured plates give convincing support to the author's contentions.

It is interesting to read in such an authoritative volume that the diagnosis of gonorrhoea can be made in most cases without the aid of cultures, particularly since culture of the gonococcus presents such practical difficulties. The differential diagnosis of smear preparations and the many pit-falls to be evaded are ably dealt with. There is a lot more in examining a urethral or cervical smear than merely deciding whether the gonococcus is present or not; and even this can be difficult, as Dr. Harkness shows. The complement fixation test for gonorrhoea which was popularized chiefly by Price at the London Hospital is subjected to critical and unfavourable comment.

While it cannot be contended that the numerous clinical conditions cusing urethritis are grave enough to be menacing, their inclusion in one volume, the detailed description of each and the abundant and excellent illustrations, make this an outstanding work. The hundreds of references to the literature are a monument to Dr. Harkness' diligence and scholarship and proof of his extensive acquaintance with this subject.

But this is not a book for the general practitioner. Its size and completeness make it rather a book of reference for the specialist who deals with affections of the male urethra. For such a reader this volume represents an almost inexhaustible source of well documented information, and thanks are due to Dr. Harkness for providing us with such a fund of knowledge.

The publishers, Messrs. E. S. Livingstone of Edinburgh, have produced a book which is a credit to British medical publications. It is beautifully printed and the arrangement of the many chapters permits this handsome volume to serve as a ready source of instruction. It can be recommended as the most comprehensive and authoritative work which has appeared under this title.

BLOOD GROUPS IN MAN

Blood Groups in Man. By R. R. Race, Ph.D. (Cantab.), M.R.C.S. (England) and Ruth Sanger, Ph.D. (London), B.Sc. (Sydney). (Pp. 290 + xv, with tables and figures. 30s.) Oxford: Blackwell Scientific Publications. 1950.

Contents: 1. Introduction. 2. Blood Groups and Human Genetics. 3 The *ABO* Blood Groups. 4. The Distribution of Blood Group Antigens in the Human Body. 5. The *MNS* Blood Groups. 6. The *P* Blood Groups. 7. The *Rh* Antigens. 8. The Inheritance of the *Rh* Blood Groups. 9. *Rh* Antibodies. 10. Methods Used in *Rh* Testing. 11. The *Lutheran* Blood Groups. 12. The *Kell* Blood Groups. 13. Secretion in the Saliva of the Antigens of the *ABO* System. 14. The *Lewis* Blood Groups. 15. The *Duffy* Blood Groups. 16 Other Blood Groups 17. Identification of Blood Group Antibodies. 18. The Multiplicity of Blood Group Combinations. 19. Blood Groups and Disease. 20. Blood Groups and Problems of Parentage and Identity

Those interested in the theoretical as well as the practical aspects of the blood groups in man will find this little volume a very readable introduction to the subject, as well as an extremely useful supplement to Wiener's magnificent treatise on *Blood Groups and Blood Transfusion.*

As is almost to be expected, the emphasis is on the Rh and other more recent blood groups. The factual account of the Rh problem is probably the most definitive available for the average reader in an easily comprehensible form. Nevertheless, some of the lines of reasoning, especially in regard to Rh terminology, are not easy to follow. The fact that Fisher's notation 'is the only one easily understandable to the reader new to the subject' (p. 82) is not an argument bearing on the validity of the notation or the hypothesis. It may well be that Wiener's notation, although a more difficult one for the beginner, is the more accurate one.

The authors make the point that the controversy about nomenclature between Wiener and Fisher concerns only the highly academic and interesting point whether the three closely-linked genes of Fisher should be placed within or without the boundary of one gene. This is certainly no academic point because if the alleles are to be placed within the boundary of one gene, the need for crossing-over in Fisher's hypothesis becomes entirely redundant and there is no need to depart from the multiple allelomorphism of Wiener's hypothesis.

The appearance of the rarer Rh types depends upon the crossing-over mechanism in the population of England, which is assumed to be relatively stable and pure genetically. It will be useful to know whether extensive investigations of large populations of anthropological interest will confirm Fisher's assumption of three closely-linked genes. The issue may well be in doubt, particularly in view of the highly suspect status at present enjoyed by anti-*d*.

The medico-legal applications are fascinating, and considerable. They are set out extremely well and the unusual employment of the antiglobulin test in connexion with paternity is referred to on page 254. The authors describe the interesting possibility that with the rarer groups such as Kell, Lutheran, Lewis, Duffy, etc., it may actually be possible positively to prove paternity beyond all reasonable doubt if the brothers of the accused can produce satisfactory alibis.

In an addendum (p. 277) the authors record a remarkable case claimed to illustrate a deletion of all genes except D on the chromosome pair concerned. The short account given does certainly not exclude the possibility of alleles at the loci C and E, not detectable with antisera at present available.

The book is a stimulating presentation of the modern concepts of the blood groups in man and will be read with enjoyment by the proponents of both schools of thought in the Rh field of study.

TROPHIC NERVES

Trophic Nerves: Their Role in Physiology and Pathology with Especial Reference to the Aetiology of Malignant, Neurological and Mental Disease and Inflammatory and Atrophic Changes. By R. Wyburn-Mason, M.A., M.D., B.Ch. (Camb.), M.R.C.P. (Lond.). (Pp. 1,083 + xi. With 69 illustrations. 75s.) London: Henry Kimpton. 1950.

Contents: 1. The Evolution of the Vertebrate Nervous System. 2. Unmyelinated Nerve Fibres and the Autonomic Pathways Within the Nervous System. 3. Afferent Pathways Affecting Autonomic Activity. 4. The Structure and Significance of Changes in the Surface Membrane of Cells. 5. The Effects of Lysing and Antilysing Agents on Cell Activity. 6. The Blood-Brain Barrier and Colloid Deposition in the Central Nervous System. 7. The Non-Specific Changes Produced in the Central Nervous System by Noxious Agents. 8. Pain and Temperature Sensibility and Unmyelinated Nerve Fibres. 9. Disturbances of Pain Sensibility. 10. Trophic Disturbances from Lesions of the Peripheral Protopathic Pain Pathways and Drug Addiction. 11. Trophic Lesions Corresponding to the Distribution of Nerve Roots and in Von Recklinghausen's Disease. 12. The Cause of Trophic Lesions and Normal Trophic Activity. 13. Trophic Disturbances from Diseases of the Central Grey Matter of the Nervous System. 14. Trophic Nerves to the Eye and Ear. 15. Cholinergic and Adrenergic Swing. 16. Sterol Bodies and Trophic Activity. 17. Further Observations on the Control of Metabolic Processes by Cholinergic and Adrenergic Nerve Fibres. The Function of Insulin. 18. The Function of White Blood Corpuscles and the Thymus Gland. 19. The Role of the Anterior Pituitary Gland. 20. The Nerve Roots Supplying Trophic Fibres to Various Tissues. 21. The Trophic and Autonomic Control of Activity in the Central Nervous System. 22. The Role of Uumyelinated Fibres in Controlling Muscle Tone and Contraction. 23. Fatigue and the Role of Trophic and Autonomic Nerves in Relation to Myelinated Fibres. 24. The Conscious Recording of Activity in Efferent Cholinergic and Adrenergic Nerve Fibres, the Nature of Protopathic Sensibility and Emotional Experience and the Effects of Emotion on the Body. 25. The General Effects of the Introduction into the Body of Non-Specific Lysing Agents. 26. The Effects on the Body of Certain Non-Specific Noxa. 27. The Effects on the Body of Certain Specific Agents. 28. The Manifestations of Adolescence, Menstruation, Pregnancy, the Menopause and Senility. 29. The Disturbance of Activity in Unmyelinated Fibres in the Production of Psychotic, Psychoneurotic, Intellectual and Certain Motor Disturbances. 30. The Trophic Centres for Somatic Tissues in the Hypothalamus and Bulb, the Trophic Pathways to the Tissues and the Trophic Centres and Pathways in the Central Nervous System. 31. Shock, the Effects of Cerebral and Spinal Concussion and the Nature of Unconsciousness. 32. Sleep. 33. The Interpretation of the Electro-Encephalogram. 34. Trophic Disturbances of the Skin, Hair and Nails. 35. The Trophic Control of Function of Bones, Teeth and Joints. 36. Trophic Changes in the Alimentary Tract. 37. The Control of the Red and White Blood Cells by the Nervous System. 38 Trophic Diseases of the Cardiovascular and Respiratory Systems. 39. Trophic Diseases of the Ear and Eye. 40. Trophic Disturbances of the Peripheral Nerves and Muscles. 41. Trophic Diseases of the Thyroid Gland and Thyrotoxicosis. 42. The Nervous Control of Renal Activity and Trophic Diseases of the Kidney and Bladder. 43. The Function of the Parathyroid Glands and Vitamin D. 44. Heredofamilial Diseases and Developmental Anomalies. 45. The Effects of Noxa on the Immature Animal, Foetus and Embryo and Their Role in Causing Developmental Anomalies. 46. Growth, Differentiation and Developmental Anomalies. 47. The Control of Differentiation in Cells. 48. The General Structure of Living Cells and Metabolic Processes of Animal and Plant Cells. 49. On the Nature of Malignant Growths. 50. The Correlation of Trophic Activity in the Brain with that in Overlying Tissues, Headache and Demyelinating Diseases. 51. The Effects of Disturbance of Function of the Sensory Pathways and Sensory Cortex. 52. The Organization of Movement in Mammals. 53. Voluntary Movement. 54. Voluntary Movement (continued). 55. The Function of the Prefrontal Areas, Excitement, Apathy and Stupor. 56. The Processes of Thought. 57. Voluntary Movements and Movements of the Eyes. 58. Some Disturbances of Trophic Control of Cerebral Function. 59. Recurrent Short-Lived Disturbances of Cortical Function, Narcolepsy, Cataplexy, Migraine, Familial Periodic Paralysis and Epilepsy. Appendix. References. Index.

This bulky volume of nearly a thousand pages of text is dedicated to the thesis of a 'single cause' for physiological activity, and ultimately for the manifestations of disease processes. Throughout the nervous system, the brain, spinal cord, peripheral nerves, and the autonomic system, there are fine unmyelinated nerve fibres, in greater or lesser numbers, and it is the author's contention that any influence acting on any tissue does so first on these fibres, before it affects other constituents and that it is the trophic function of these unmyelinated nerve fibres which produces the 'cholinergic' and 'adrenergic' nervous activity and the vasodilator effects which are the ultimate basis for all functional activity, and its disturbances which occur under pathological conditions.

An hypothesis which sets out to explain phenomena, even though it may not yet be capable of complete proof by experiment and scientific deduction on the basis of factual evidence, may nevertheless well be acceptable and form the theme for a project in research; but it is certainly necessary that facts should not be distorted nor should interpretations be forced in such a way as to fit a thesis.

Throughout the book the author makes statements, emphasizes some aspects of an observation, ignores others contrary to generally accepted views, in order to establish his conclusions so as to fit his generalization. For example, in discussing the problem of the local vulnerability of the nervous system, after stating the various current ideas on the subject, which are quite reasonably found to be somewhat inadequate, he states that because the vulnerable areas correspond largely to the areas of greatest capillary permeability within the nervous system, they are in fact the regions where the unmyelinated and autonomic fibres are chiefly aggregated. Is this a fact? Again, in dealing with the role of the anterior pituitary he states: 'Pregnancy may be followed not only by acromegaly, but also by Simmonds' disease. The latter syndrome occurring in such conditions is usually ascribed to vascular thromboses in the gland, but the fact that acromegaly may also occur in the same condition makes this unlikely.'

The author repeatedly makes claims in this manner and as one ploughs through the heavy reading involved this only tends to increase doubt rather than to impress with any conviction the thesis he sets out to prove. In fact, the vague and discursive style, the bad arrangement of subject matter, the repetitions under different headings, all do the subject a disservice and the author would have done better to have written a smaller book confining himself to the known facts instead of demonstrating the undoubted erudition and great industry involved in the production of this weighty tome.

The publishers have served the author well, the paper and type are excellent and very few printer's errors were discovered.

CORRESPONDENCE

S.A. ASSOCIATION FOR HEALTH, PHYSICAL EDUCATION AND RECREATION

To the Editor: At the S.A. Congress for Physical Education held in Cape Town in January of this year the above-named Association was formed. This National Association can only function with the assistance of the Provincial Branches, which again cannot function without the assistance of clubs, associations, etc., in the Province as well as all individual members who are interested in any aspect of health, physical education and recreation.

The object is to promote interest in this field and to co-operate with those entrusted with the advancement of health, physical education and recreation; with the assistance of all persons interested we are convinced we can do very useful work.

At the General Meeting of the W.P. Branch of the Association held in May 1950, the following Committee was elected: Capt. G. Barber, Dr. S. Shulman, Mr. Wahl, Mr. Paincyk, Miss Niland.

Since then the Committee has met and formulated a policy and has now reached the stage when a special general meeting is to be called to put the Association on a sound footing in regard to passing of the Constitution. etc.

It is hoped that this Association will have your full support, in view of the fact that it aims at co-ordinating and interesting the general public with regard to the benefits of health and recreation.

(Miss) W. Niland,
Honorary Secretary.

Western Province Branch,
P.O. Box 652,
Cape Town.
17 October 1950.

REMUNERATION OF MEDICAL OFFICERS

To the Editor: In the current issue of the *Journal*, there is an advertisement for a position as Medical Officer to the Ancient Order of Foresters, Pietermaritzburg. The remuneration paid by this Order is completely at variance with the tariff of fees laid down for Medical Aid Societies.

I feel that any organization advertising for a medical officer should submit the conditions of service and remuneration to you for your consideration and approval, before advertising such posts.

'Indignant.'

30 October 1950.